

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously presented) A microcapsule comprised of:

a plurality of internal, immiscible liquid phases;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and

one or more energy absorbing trigger particles contained in an internal liquid phase in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles are co-encapsulated with the plurality of internal, immiscible liquid phases by the flexible polymer outer membrane, wherein the one or more energy absorbing trigger particles sediment in the internal liquid phase in contact with the polymer outer membrane, wherein at least one of the one or more energy absorbing trigger particles are in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles have a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and wherein the temperature of the one or more energy absorbing trigger particles is increased by absorbing the energy to melt at least a portion of the polymer outer membrane.

2-5. (Cancelled)

6. (Currently amended) The microcapsule of claim 1, wherein the polymer outer membrane comprises ~~glycerol~~ polyvinyl alcohol and the one or more energy absorbing trigger particles comprises aluminum powder.

7-29. (Cancelled)

30. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 1 to about 500 microns.
31. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 300 to about 500 microns.
32. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 50 to about 300 microns.
33. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 30 to about 50 microns.
34. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 20 to about 30 microns.
35. (Original) The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 1 to about 20 microns.
36. (Cancelled)
37. (Currently amended) The microcapsule of claim 77, wherein the radiocontrast media is a halogenated oil, wherein the one or more energy absorbing trigger particles comprises aluminum powder, and wherein the flexible polymer outer membrane comprises polymer alcohol.
38. (Withdrawn) The microcapsule of claim 37 wherein the halogenated oil is poppy seed oil, cotton seed oil, soybean oil, safflower oil, corn oil, sunflower seed oil, sesame seed oil, or canola oil.

39. (Original) The microcapsule of claim 37, wherein the radiocontrast media is iodinated poppy seed oil.

40. (Original) The microcapsule of claim 1, contained in a pharmaceutically acceptable solution.

41-42. (Cancelled)

43. (Withdrawn) The composition of claim 78, wherein said first portion contains a different drug than said second portion.

44. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and one or more energy absorbing components selected from the group consisting of amorphous carbon, graphite, aluminum powder, acetylene black, sodium amyl alcohol, sorbitan monoleate, 2% sorbitan monooleate/20 moles ethylene oxide, and paraffin oil, in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

45-48. (Cancelled)

49. (Withdrawn) The method of claim 79, wherein the electromagnetic field is an electromagnetic field with a frequency of from about 20 to about 500 KHz.

50. (Withdrawn) The method of claim 79, wherein the electromagnetic field is an electromagnetic field with a frequency of from about 85 to about 100 KHz.

51-54. (Cancelled)

55. (Withdrawn) The method of claim 81, wherein the microcapsules are administered to a subject and detected at a target site by radiography, prior to heating the internal component.

56. (Withdrawn) The method of claim 44, wherein the microcapsules are administered to a subject intraarterially, intravenously, intraperitoneally, directly into a tissue, or directly into a tumor.

57-72. (Cancelled)

73. (Previously presented) A microcapsule comprised of:

- one or more internal, immiscible liquid phases;
- a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and
- a spheroid of one or more energy absorbing trigger particles in an internal liquid phase in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles sediment in the internal liquid phase in contact with the polymer outer membrane, and wherein at least one of the one or more energy absorbing trigger particles is in contact with the polymer outer membrane, wherein the spheroid has a higher specific absorption rate for ultrasound energy than the specific absorption rate of the polymer outer membrane, and wherein the temperature of the spheroid is increased by absorbing the energy to melt at least a portion of the polymer outer membrane.

74. (Previously presented) A microcapsule comprised of:

one or more internal, immiscible liquid phases, wherein the liquid phases are comprised of at least one internal aqueous phase and at least one internal hydrocarbon phase;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and

one or more energy absorbing trigger particles in an internal liquid phase in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles sediment in the internal liquid phase in contact with the polymer outer membrane, and wherein at least one of the one or more energy absorbing trigger particles is in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles have a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer membrane, and wherein the temperature of the one or more energy absorbing components is increased by absorbing the energy to melt at least a portion of the polymer outer membrane.

75. (Withdrawn) A microcapsule consisting of:

one or more internal, immiscible liquid phases;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and

one or more energy absorbing trigger particles selected from the group consisting of amorphous carbon, graphite, and aluminum powder, in an internal liquid phase in contact with the outer membrane; and

a drug or drug precursor in the internal liquid phase in contact with the outer membrane,

wherein the one or more energy absorbing trigger particles sediment in the internal liquid phase

in contact with the polymer outer membrane,

wherein at least one of the one or more energy absorbing trigger particles is in contact with the polymer outer membrane,

wherein the one or more energy absorbing trigger particles have a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and
wherein the temperature of the one or more energy absorbing trigger particles is increased by absorbing said energy to melt at least a portion of the polymer outer membrane.

76. (Withdrawn) A microcapsule consisting of:

- one or more internal, immiscible liquid phases;
- a flexible polymer outer membrane encapsulating the liquid phase, the polymer outer membrane having a melting temperature; and
- one or more energy absorbing trigger particles selected from the group consisting of amorphous carbon, graphite, and aluminum powder, contained in a first internal liquid phase;
- a drug precursor in a the first internal liquid phase; and
- an activator of said drug precursor in a second internal liquid phase immiscible with the first internal liquid phase,

wherein the first internal liquid phases is in contact with the outer membrane,
wherein the one or more energy absorbing trigger particles sediment in the first internal liquid phase in contact with the polymer outer membrane,
wherein at least one of the one or more energy absorbing trigger particles is in contact with the polymer outer membrane,
wherein said one or more energy absorbing trigger particles have a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and
wherein the temperature of said one or more energy absorbing trigger particles is increased by absorbing said energy to melt at least a portion of the polymer outer membrane.

77. (Previously presented) A microcapsule comprised of:

- one or more internal, immiscible liquid phases;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and

one or more energy absorbing trigger particles containing a radiocontrast media, in an internal liquid phase in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles sediment in the internal liquid phase in contact with the polymer outer membrane, and wherein at least one of the one or more energy absorbing trigger particles is in contact with the polymer outer membrane, wherein the one or more energy absorbing trigger particles have a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and wherein the temperature of the one or more energy absorbing trigger particles is increased by absorbing the energy to melt at least a portion of the polymer outer membrane.

78. (Cancelled)

79. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and one or more energy absorbing components in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

80. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting

temperature, and one or more energy absorbing components in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component consists of a spheroid within the microcapsule, and wherein the energy is ultrasound, wherein the energy absorbing component has a higher specific absorption rate for ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

81. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and one or more energy absorbing components in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases, wherein the microcapsules contain a drug precursor in a first internal liquid phase and an activator of the drug precursor in a second internal liquid phase immiscible with the first internal liquid phase;

exposing the microcapsules to an energy source effective to mix the immiscible internal liquid phases and increase the kinetics of activation of the drug precursor prior to heating the magnetic particles;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

82. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and one or more energy absorbing components selected from the group consisting of amorphous carbon, graphite, aluminum powder, acetylene black, sodium amyl alcohol, sorbitan monooleate, 2% sorbitan monooleate/20 moles ethylene oxide, and paraffin oil, in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases, and wherein the microcapsules contain a radiocontrast medium;

wherein the microcapsules are administered to a subject intraarterially, intravenously, intraperitoneally, directly into a tissue, or directly into a tumor;

administering the drug delivery solution to a subject; and

detecting said microcapsules at a target site by radiography, prior to heating the internal component;

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

83-84. (Cancelled)

85. (Previously presented) A microcapsule comprised of:

two to four internal, immiscible liquid phases;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature;

an energy absorbing trigger particle in an internal liquid phase in contact with the polymer outer membrane, and

a drug or drug precursor, in an internal liquid phase not in contact with the polymer outer membrane,

wherein the energy absorbing trigger particle sediments in the internal liquid phase in contact with the polymer outer membrane,

wherein the energy absorbing trigger particle is in contact with the polymer outer membrane,

wherein the energy absorbing trigger particle has a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and

wherein the temperature of the energy absorbing trigger particle is increased by absorbing the energy to melt at least a portion of the polymer outer membrane.

86. (Withdrawn) A microcapsule consisting of:

two to four internal, immiscible liquid phases;

a flexible polymer outer membrane encapsulating the liquid phases, the polymer outer membrane having a melting temperature; and

an energy absorbing trigger particle selected from the group consisting of amorphous carbon, graphite, and aluminum powder, in a second internal liquid phase;

a drug precursor in a first internal liquid phase; and

an activator of said drug precursor in a second internal liquid phase immiscible with the first internal liquid phase,

wherein the second internal liquid phases is in contact with the outer membrane,

wherein the energy absorbing trigger particle sediment in the second internal liquid phase in contact with the polymer outer membrane,

wherein the energy absorbing trigger particle is in contact with the polymer outer membrane,

wherein said energy absorbing trigger particle has a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer outer membrane, and

wherein the temperature of said energy absorbing trigger particle is increased by absorbing said energy to melt at least a portion of the polymer outer membrane.

87. (Cancelled)

88. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of two to four internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and an energy absorbing component selected from the group consisting of amorphous carbon, graphite, aluminum powder, acetylene black, sodium amyl alcohol, sorbitan monooleate, 2% sorbitan monooleate/20 moles ethylene oxide, and paraffin oil, in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the energy absorbing component and to melt at least a portion of the polymer outer membrane and to release the drug.

89. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of two to four internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and an energy absorbing component in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases, wherein the microcapsules contain a drug precursor in a first internal liquid phase and an activator of the drug precursor in a second internal liquid phase immiscible with the first internal liquid phase;

exposing the microcapsules to an energy source effective to mix the immiscible internal liquid phases and increase the kinetics of activation of the drug precursor prior to heating the magnetic particles;

administering the drug delivery solution to a subject; and
exposing the microcapsule to an energy source, effective to heat the energy absorbing component and to melt at least a portion of the polymer outer membrane and to release the drug.

90. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of two to four internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and an energy absorbing component in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and
exposing the microcapsule to an energy source, effective to heat the energy absorbing component and to melt at least a portion of the polymer outer membrane and to release the drug.

91. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of two to four internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and an energy absorbing component in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component consists of a spheroid within the microcapsule, and wherein the energy is ultrasound, wherein the energy absorbing component has a higher specific absorption rate for ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and
exposing the microcapsule to an energy source, effective to heat the energy absorbing component and to melt at least a portion of the polymer outer membrane and to release the drug.

92. (Withdrawn) A method of controlling the release of a drug consisting of:

providing a drug delivery solution consisting of microcapsules consisting of two to four internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and an energy absorbing component selected from the group consisting of amorphous carbon, graphite, aluminum powder, acetylene black, sodium amyl alcohol, sorbitan monooleate, 2% sorbitan monooleate/20 moles ethylene oxide, and paraffin oil, in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for electromagnetic, radiofrequency, microwave, or ultrasound energy than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal phases, and wherein the microcapsules contain a radiocontrast medium;

wherein the microcapsules are administered to a subject intraarterially, intravenously, intraperitoneally, directly into a tissue, or directly into a tumor;

administering the drug delivery solution to a subject;

detecting said microcapsules at a target site by radiography, prior to heating the energy absorbing component; and

exposing the microcapsule to an energy source, effective to heat the energy absorbing component and to melt at least a portion of the polymer outer membrane and to release the drug.

93. (Previously presented) The microcapsule of claim 1, wherein all mixing between the internal, immiscible liquid phases is substantially limited.

94. (Previously Presented) The microcapsule of claim 1, wherein the internal, immiscible liquid phases comprise multi-lamellar phases.

95-96. (Cancelled)

97. (Previously presented) The microcapsule of claim 1, further comprising a drug or drug precursor in the liquid phase in contact with the polymer outer membrane.

98. (Previously presented) The microcapsule of claim 97, wherein the drug or drug precursor is an anti-cancer drug or anti-cancer drug precursor.
99. (Withdrawn) The microcapsule of claim 98, wherein the anti-cancer drug is cis-platin, doxorubicin, daunorubicin, diaziquone, paclitaxel, aziridinylbenzoquinone, muramyltriptide, 5-fluorouracil, cyclophosphamide, melphalan, dacarbazine, methotrexate, cytarabine, azaribine, mercaptopurine, thioguanine, vinblastine, vincristine, bleomycin, prednisone, ethinyl estradiol, diethylstilbestrol, tamoxifen, testosterone propionate, or fluoxymesterone.
100. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is an anesthetic.
101. (Withdrawn) The microcapsule of claim 100, wherein the anesthetic is cocaine, procaine, or lidocaine.
102. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is a systemic antibiotic.
103. (Withdrawn) The microcapsule of claim 102, wherein the antibiotic is a penicillin, vancomycin, a cephalosporin, erythromycin, ampicillin, amoxicillin, chloramphenicol, rifampicin, gentamicin, sulfanilamide, sulfadiazine, sulfamethoxazole, sulfisoxazole, sulfacetamide, para-aminobenzoic acid, streptomycin, or isoniazid.
104. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is a systemic antifungal.
105. (Withdrawn) The microcapsule of claim 104, wherein the antifungal is nystatin, or amphotericin B, or griseofulvin.

106. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is a systemic antiviral.

107. (Withdrawn) The microcapsule of claim 106, wherein the antiviral is idoxuridine, iododeoxuridine, riboviran, or amantidine.

108. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is an anti-parasitic.

109. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is an anti-inflammatory.

110. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is a hormone, a steroid, hydrocortisone, dexamethasone, a systemic quinolone, an aminoglycoside, an antidote, an anti-cholinesterase, a metal poisoning antidote, a cytotoxic agent, an immunomodulator, a cytokine, an interleukin, an alpha-antitrypsin, a bone metabolism regulator, a hypercalcemic agent, a cardiovascular agent, a beta blocker, a cerebral vasodilator, a cerebral metabolic enhancer, a colony stimulating factor, a granulocyte-colony stimulating factor, a granulocyte macrophage-colony stimulating factor, a vasopressor, a local diabetic agent, a CT scan enhancer, an angiocardiology agent, an adenosine deaminase deficiency agent, a gonadotropin inhibitor, an adrenal cortical steroid inhibitor, a gonadotropin releasing hormone stimulant, a urofollitropin, a muscle relaxant, a neuromuscular blocking agent, a prostaglandin analog, a prostaglandin, a prostaglandin inhibitor, a respiratory therapy agent, an anticholinergic, a beta andrenergic stimulator, a metoclopramide, tetrahydrocannabinol or a sympathomimetic.

111. (Withdrawn) The microcapsule of claim 97, wherein the drug or drug precursor is a thrombolytic agent.

112. (Withdrawn) The microcapsule of claim 111, wherein the thrombolytic agent is urokinase (uPA), tissue plasminogen activator (tPA) or streptokinase.

113. (Previously presented) The microcapsule of claim 1, wherein the plurality of internal, immiscible liquid phases is comprised of two to four internal, immiscible liquid phases and further comprising:

a drug precursor in a first internal liquid phase; and

an activator of the drug precursor in a second internal liquid phase immiscible with the first internal liquid phase,

wherein the internal liquid phase in contact with the polymer outer membrane is the second internal liquid phase.

114. (New) The microcapsule of claim 73, wherein the flexible polymer membrane comprises polymer alcohol and the one or more energy absorbing trigger particles comprises aluminum powder.

115. (New) The microcapsule of claim 74, wherein the flexible polymer membrane comprises polymer alcohol and the one or more energy absorbing trigger particles comprises aluminum powder.

116. (New) The microcapsule of claim 85, wherein the flexible polymer membrane comprises polymer alcohol and the one or more energy absorbing trigger particles comprises aluminum powder.